Agios Submits sNDA to FDA for U.S. Accelerated Approval of Mitapivat in Sickle Cell Disease

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- sNDA submission follows agreement with FDA on confirmatory trial, a requirement of the accelerated approval pathway
- Confirmatory trial designed to demonstrate clinical benefit of mitapivat on reducing transfusion burden in sickle cell disease

CAMBRIDGE, Mass., May 12, 2026 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a commercial-stage biopharmaceutical company focused on delivering innovative medicines for patients with rare diseases, today announced the submission of its supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for the U.S. accelerated approval of mitapivat, an oral pyruvate kinase (PK) activator, in sickle cell disease. The submission follows agreement with the FDA on the confirmatory clinical trial, which is required under the accelerated approval pathway.

The confirmatory clinical trial is designed to demonstrate the clinical benefit of mitapivat on reducing transfusion burden in sickle cell disease, with a primary endpoint of transfusion free from Week 4 through Week 52. The global, randomized, double-blind, placebo-controlled, 52-week trial will enroll approximately 159 patients aged 12 years or older with sickle cell disease. The design of the confirmatory trial is informed by a clinically meaningful reduction in transfusion burden that was observed with mitapivat compared to placebo in the RISE UP Phase 3 trial based on data systematically and prospectively collected. These results will be included in an oral presentation on the RISE UP Phase 3 trial during the Plenary Abstracts Session at the 31st European Hematology Association (EHA) Congress on June 13, 2026, in Stockholm, Sweden.

“The submission of the mitapivat sNDA represents an important milestone for the sickle cell community, which urgently needs new treatments that can address key underlying aspects of this debilitating and deadly disease,” said Sarah Gheuens, M.D., Ph.D., Chief Medical Officer and Head of R&D, Agios. “The sNDA is supported by data from the RISE UP clinical program demonstrating that mitapivat significantly improved hemoglobin concentration and reduced hemolysis in patients with sickle cell disease, translating into clinically meaningful benefits in pain crises and related hospitalizations, as well as fatigue, for those who achieved a hemoglobin response. This strong anti-hemolytic profile builds on clinical data that supported regulatory approvals in two other rare hemolytic anemias. We believe mitapivat is well-positioned to become the first PK activator approved in the U.S. for sickle cell disease, and we look forward to continued engagement with the FDA throughout the review process.”

The mitapivat sNDA is based on data from the global, randomized, double-blind, placebo-controlled RISE UP Phase 2 and Phase 3 trials. Agios expects to receive notice of the sNDA filing acceptance and anticipated review timeline in the third quarter of 2026, following the FDA’s 60-day filing review period.

About U.S. Accelerated Approval
The U.S. Food and Drug Administration’s (FDA) accelerated approval pathway expedites the availability of medicines that can fill a medical need for a serious condition. A confirmatory clinical trial is required to convert the accelerated approval to a traditional approval, and this trial must be underway when the FDA makes its approval decision.

About Sickle Cell Disease
Sickle cell disease is a rare, inherited blood disorder caused by the production of abnormal hemoglobin that disrupts the ability of red blood cells to carry oxygen throughout the body. As a result, red blood cells become rigid and sickle-shaped, causing deformation of red blood cell membranes and the premature death of the cells. These effects lead to chronic hemolytic anemia, vaso-occlusion, and a cascade of severe and life-threatening complications, including long-term damage to the lungs, kidneys, and cardiovascular system. Due to its physical toll, sickle cell disease imposes a profound burden on patients and their families, marked by increased healthcare needs and early mortality.

About Mitapivat in Sickle Cell Disease
Mitapivat, an oral pyruvate kinase (PK) activator, is designed to enhance the process by which red blood cells produce energy. This approach has the potential to improve red blood cell health by increasing ATP levels to support increased energy demands and lowering levels of a molecule called 2,3-diphosphoglycerate (2,3-DPG). In sickle cell disease, increased stress on red blood cells results in elevated levels of 2,3-DPG, which raises the likelihood that red blood cells develop the abnormal “sickle” shape that triggers vaso-occlusive crises.

About the RISE UP Phase 3 Trial Topline Results
The global RISE UP Phase 3 trial (NCT05031780) is evaluating the efficacy and safety of mitapivat in sickle cell disease patients aged 16 years or older, representative of the global population. The trial consisted of a 52-week, double-blind, randomized, placebo-controlled period, in which 207 participants were randomized 2:1 to receive oral mitapivat (100 mg) twice daily (n=138) or matched-placebo (n=69). Upon completion, participants could transition into an open-label extension (OLE) period where all receive mitapivat.

To comprehensively evaluate objective measures of hemolysis alongside other clinically relevant outcomes in sickle cell disease, the double-blind period of RISE UP included two primary endpoints – hemoglobin response and annualized rate of sickle cell pain crises – as well as five key secondary endpoints measuring hemoglobin concentration, indirect bilirubin (a biomarker of hemolysis), patient-reported fatigue, hospitalizations for sickle cell pain crises, and percent reticulocyte levels (a biomarker of erythropoiesis).

Mitapivat demonstrated a statistically significant improvement compared to placebo in the study’s primary endpoint of hemoglobin response, defined as a ≥1.0 g/dL increase from baseline in average hemoglobin concentration from Week 24 through Week 52. Although mitapivat showed a reduction in the annualized rate of sickle cell pain crises compared with placebo, this primary endpoint did not reach statistical significance.

Patients receiving mitapivat who achieved the hemoglobin response primary endpoint had clinically meaningful improvements in hemoglobin concentration. These patients also experienced other clinically meaningful benefits, including reductions in pain crises and related hospitalizations,

along with improvements in fatigue.

The safety profile was consistent with prior mitapivat trials in sickle cell disease. The 52-week double-blind period was completed by 87.0% (n=120/138) of patients in the mitapivat arm and 81.2% (n=56/69) of patients in the placebo arm. All but two of these patients (174/176) opted to enter the ongoing OLE period of the trial.

About Agios: Fueled by Connections to Transform Rare Diseases™
At Agios, our vision is to redefine the future of rare disease treatment. Fueled by connections, we build trusted partnerships with communities – collaborating to develop and deliver innovative medicines that have the potential to transform lives. With a foundation in hematology, we combine biological expertise with real-world insights to advance a growing pipeline of rare disease medicines that reflect the priorities of the people we serve. Agios is a commercial-stage biopharmaceutical company headquartered in Cambridge, Massachusetts. To learn more, visit www.agios.com and follow us on LinkedIn and X.

Available Information about Agios
To achieve broad dissemination, Agios may disclose information to the public through a variety of disclosure channels including press releases, SEC filings, and public conference calls and webcasts. Some of the information distributed through these disclosure channels may be considered material information. Investors and others should note that Agios plans to use its website (www.agios.com) as a distribution channel to announce and give notice of Agios' upcoming events and presentations (including, but not limited to, presentations at medical or healthcare conferences). Such information, which may be deemed material, will be available on the Investors section of the company's website under the "Events & Presentations" tab. In addition, you may sign up to automatically receive email alerts about Agios' upcoming events and presentations ("Calendar Alerts") by visiting the "Email Alerts" option under the "IR Resources" tab of the Investors section of the company's website and submitting your email address.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding the potential benefits of mitapivat; Agios' expectations for the review of its sNDA for mitapivat by the FDA; and the potential benefits of Agios' strategic plans and focus. The words "anticipate," "expect," "goal," "hope," "milestone," "plan," "potential," "possible," "strategy," "will," "vision," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Agios' current expectations and beliefs. For example, there can be no guarantee that any product candidate Agios is developing will successfully commence or complete necessary preclinical and clinical development phases, or that development of any of Agios' product candidates will successfully continue. There can be no guarantee that any positive developments in Agios' business will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other important factors, including, without limitation: risks and uncertainties related to the impact of pandemics or other public health emergencies to Agios' business, operations, strategy, goals and anticipated milestones, including its ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products; Agios' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA, the EMA or other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Agios' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures; competitive factors; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; Agios' ability to establish and maintain key collaborations; uncertainty regarding any royalty payments related to the sale of its oncology business or any milestone or royalty payments related to its in-licensing of AG-236, and the uncertainty of the timing of any such payments; uncertainty of the results and effectiveness of the use of Agios' cash and cash equivalents; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' public filings with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Agios expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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